MEDICAL DEVICES:

The Relationship Between TRADE *and* REGULATIONS

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Introduction

The globalization of the medical device industry over the past 20 years requires competitive US medical device firms to focus not only on the domestic market but the global market as well. Since the US market is growing 5% to 6% annually and many of the emerging markets are growing between 10% and 20% annually, the US medical device suppliers should pay particular attention to opportunities in these emerging markets.

Regulatory affairs professionals working for US medical device firms often contact the Department of Commerce with specific questions about regulations in developing countries. They are often perplexed at redundant or ambiguous requirements. Sometimes the department's International Trade Administration (ITA) is able to provide the answers. At other times, ITA can only give background information on larger political issues affecting the market in question and direct policy efforts toward encouraging the foreign government to implement regulations more favorable for trade. While the Commerce Department recognizes the right of foreign governments to protect the health and safety of their medical device delivery systems, free trade often results in increased patient access to medical technology and is ultimately in the interest of the foreign governments and its citizens. In trying to attain and maintain compliance, working with foreign governments and agents, as well as internal marketing and product development departments, the regulatory affairs professional stands to benefit from a better understanding of the relationship between international trade and trends in device regulation and reimbursement.

Our trading partners' regulatory and reimbursement policies and procedures have a vast impact on interna-tional trade of medical devices, and in turn affect the cost of healthcare and patient access to medical technologies. Some nations have well-established, transparent medical device regulatory and reimbursement systems. In more affluent countries, which also usually have more transparent regulatory systems, citizens enjoy a higher standard of health care. Governments of many developing nations also are trying to be more responsive to citizens' demands for improved access to health care and are importing more medical devices than ever before. Often, these are the same nations that are in the process of developing medical device regulatory and reimbursement systems. Unfortunately, the new regulations are sometimes inconsistent and opaque. This results in high healthcare costs, restricted patient access to advanced medical technologies and presents challenges for the medical device exporter.

The cost for medical device companies to comply with many different regulatory systems, each with its own requirements, is extremely high. Therefore, more similarity and harmony among global regulatory systems will reduce health care costs and ultimately reduce medical device prices, thus granting better access to effective and efficient healthcare.

This article explores:

- Why global medical device regulatory harmonization is important;
- What impact harmonization will have on healthcare costs and the access to modern medical technologies; and
- How regulations and trade are interrelated.

The article also reviews several nations/economies as examples of open or restrictive medical device regulatory environments and the impact these regulatory systems have on medical device trade.

Global Harmonization

The need for efficiency in the application of regulatory controls has induced national control authorities, usually a health ministry, to search for harmonized approaches to regulation and to enter into bilateral mutual recognition agreements and other international arrangements. These activities have served to foster compatibility among diverse regulatory systems. The convergence of these regulatory controls, along with the independent work of international standards-setting organizations, can enhance public health protection and enable the worldwide trade of medical products. In recognition of the growing need for international harmonization of medical device regulatory controls, senior government officials and representatives from the regulated industry in the US, EU, Canada, Japan and Australia are working to harmonize regulations through the medical device Global Harmonization Task Force (GHTF).

The US medical device industry — as well as the medical device industries in other developed nations — has the goal of "approved once, accepted everywhere." This means the industry desires that if one of the nations participating in the GHTF accepts a medical product based upon its regulatory system, then all other member countries will accept the product without further testing or review. Industry also hopes developing countries, which are establishing regulatory systems, also will accept medical devices without further review, if approved by a nation participating in the GHTF.

The medical device GHTF is clearly a step towards global harmonization. Through four study groups, the task force's goal is for regulators and industry representatives of the five members to reach agreement on common regulatory procedures. The next GHTF meeting is scheduled for September 2000 in Ottawa, Canada.

Another important GHTF feature is the effort to include developing economies. During the June 1999 GHTF meeting in Bethesda, MD, the Asian Working Party had its third meeting. The Asian group is attempting to establish formal operational procedures. The Latin American Working Party, which had its first meeting during the June GHTF meeting, is just getting started.

The more differences there are between the various national regulatory systems, the more money and staff resources that medical device firms need to spend to comply with numerous and often overlapping requirements. For example, most nations have their own requirements for clinical trials. A universal set of requirements for medical device clinical trials that satisfy all nations would be a tremendous benefit to the medical device industry. Since clinical trials are so expensive in regulatory settings, medical device manufacturers frequently exceed the requirements for any one country or economy, so the results can be used in all submissions — a costly way to operate.

The goal of all regulatory systems is to keep unsafe medical devices off the market. The Food and Drug Administration system does an excellent job in protecting US citizens from unsafe products, but is it logical to expect that all nations can adopt systems comparable to FDA? Since the FDA system is very labor intensive and requires a high level of resources and technical expertise, adoption of this

system could be out of reach for developing nations. Many countries, therefore, rely directly upon FDA decisions in deciding whether to admit medical devices for entry into their countries. But developing countries, such as Ukraine, Poland, Hungary and the Czech Republic, are modeling their regulatory systems on the EU's system. The EU system relies on third party organizations called Notified Bodies, sanctioned by the government, for plant inspection and product approval. The EU Medical Device Directive states Notified Bodies review products based upon harmonized standards, such as the globally recognized standards. However, the extensive use of nongovernmental entities is a concern for FDA. An alternative presented by FDA at an October 1999 Pan American Health Organization conference calls for a four-point program of import controls, premarket controls, quality systems and vigilance systems.

Transparency/Local Preference/ High Registration Fees

International trade professionals use the word *transparency* to describe the degree to which a regulatory system is clear and easy to understand. A good example of a transparent regulatory system is FDA. The agency's procedures are publically disclosed, consistent and evenly applied to domestic and foreign companies. FDA also has an office (Division of Small Manufacturers Assistance) devoted to helping small businesses understand what the requirements are. Receiving FDA approval is a rigorous exercise, but it is quite clear how to go about it, and procedures are applied consistently for all firms and each application.

Obtaining product approvals in a transparent system is not always easy or simple, but the firm can easily obtain the required forms, seek guidance and be faced with a consistent review process. By contrast, medical device firms seeking product approval in nations with non-transparent regulatory systems often face problems obtaining the current forms, or getting accurate information. The rules constantly change in a non-transparent regulatory system and there is often a lack of consistency from one review to the next.

To a large degree, the member countries of the Global Harmonization Task Force have transparent regulatory systems; however, many developing nations, such as Russia and Ukraine, do not.

Another concern often expressed by US medical device firms is purchasing preferences given to local medical device producers that take the form of easier product approvals or lower fees. US medical device firms also frequently complain of high registration fees and excessive review times for product approval in many developing countries.

Lack of transparency, high registration fees and local preferences are all factors that add to the cost of doing business in a particular nation and usually result in higher medical device prices. Often, government officials in developing nations assume western medical device firms will absorb the cost, but this is not the case. Furthermore, if market conditions are sufficiently unattractive, western firms may avoid the market altogether.

Cost Containment/Reimbursement

Another trend limiting access to many foreign markets is cost containment, which caps the amount paid for specific medical devices or limits the reimbursement for a medical procedure. Obviously, controlling healthcare costs is important, but if improperly implemented, a government's regulatory or reimbursement policy could have the opposite effect and could increase healthcare costs or make certain medical technologies unavailable. One common practice in developing countries to control cost is setting maximum prices, mandatory price reductions or maximum reimbursement rates for medical procedures. However, the price for a particular medical device might result in lower overall costs. Use of advanced medical devices might result in outpatient treatment instead of inpatient treatment or shorten or eliminate hospital stays. In addition, use of more advanced medical technology could result in early diagnoses, which reduces the need for more expensive follow-up treatment as well as provides more efficient healthcare services that can treat more patients per day. Health care costs can be lowered in terms of resources used per-patient and can reduce operational cost as a whole. When a price cap or reimbursement rate is too low, the medical device producer might decide not to sell in a particular nation and its citizens are denied access to this medical product or procedure.

Review of the Relationship Between Trade and Regulation in Several Nations

The rest of this article examines the regulatory systems in several important nations that represent different aspects of the global regulatory environment. The EU has a transparent regulatory system, which many developing nations are using as a model for their new medical device regulatory systems. Brazil is an example of a nation that recently established a new regulatory system but still has some regulatory problems. In addition, Russia and Ukraine represent examples of nations with non-transparent medical device regulatory systems that are taking steps toward

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improvement.

European Union (EU)

The EU is the US's largest regional export market accounting for 46% of US medical device exports and 26% of the global medical device market. The EU medical device market is $24 billion and grew by 6% in 1998. The EU has an open regulatory system for medical devices, which is transparent, based upon harmonized standards and a single system for all EU members. Medical devices sold within the EU must meet the health and safety requirements of the EU Medical Device Directive (93/42/EEC). This directive consolidates regulatory requirements within EU member nations under one system, meaning if the device can be sold in one nation, it is approved for sale in all EU countries.

The EU system is predicated on standards, in which product approvals are based on evaluations of safety and effectiveness of a device. If a product satisfies the requirements of the directive, the manufacturer can affix the "CE mark" to the product, indicating it can legally enter the commerce of any EU member. If a product comes under the jurisdiction of more than one EU directive, it must meet the requirements of all the applicable directives before it can receive the CE mark. For example, electrical medical devices must meet the requirements of both the Medical Devices Directive as well as Directive 84/539/EEC, which relates to electro-medical equipment used in human or veterinary medicine.

Product reviews and plant inspections are conducted by Notified Bodies, which are organizations sanctioned by the EU and member countries to approve medical device dossiers and manufacturing facilities. Each EU Notified Body is authorized by a member country and is under the direction of the Competent Authority of that country.

In addition to the CE mark, medical devices sold in the EU also must have a Declaration of Conformity. In addition to the requirements of the EU medical devices directive, member nations also may have their own national standards, in particular with regard to language used in product labeling.

Developments in both FDA's regulations covering Good Manufacturing Processes (GMP) and the EU Medical Device Directive (MDD) can be seen as part of a movement toward harmonization of regulatory processes and requirements in an effort to diminish trade barriers. Both the EU MDD and FDA have adopted a harmonized international management systems standard for design control and manufacturing. (ISO 13485, with minor variations in the US and EU).

The US/EU Mutual Recognition Agreement (MRA), which is initially a three-year confidence-building agreement, provides an alternate way for US medical devices to enter the European market. The MRA recognizes that certain Conformity Assessment Bodies (CABs) in the United States can conduct — in accordance with European regulatory requirements — product-approval reviews and quality-system evaluations that are equivalent to those conducted by the EU MDD. Similarly, it recognizes that CABs in the EU can conduct preliminary product approvals reviews for listed medical devices and evaluations according to FDA requirements. The MRA is anticipated to be continued after the three-year, confidence-building period, as the US and EU develop confidence in the safety of each other's system.

The US industry's perspective is that the EU is a favorable regulatory environment for medical devices. In general, US firms view the EU regulatory process as transparent with reviews being conducted in a consistent manner. In fact, since it often takes less time to obtain a CE mark than FDA approval for new class III devices, many US manufacturers obtain an EU CE mark so they can gain experience in the marketing of their product in Europe before offering it in the US market.

China

China is the world's most populous nation with 20% of the planet's population. The sheer size of medical device sales ($1.2 billion in 1998) and the potential for significant growth make China an essential sales prospect for all medical exporters that pursue a global presence.

However, while upper level management and marketers are often enthusiastic about prospective sales, China can pose a significant challenge to regulatory affairs professionals. Most device companies rely on in-country agents and distributors to handle compliance issues. This is by far the easiest arrangement, since distance and language limits US-based regulatory affairs staff's ability to obtain registra-

tion and certification requirements, make submissions, and be responsive to requests from controlling authorities in a timely manner. However, the regulatory affairs department rarely has any say in the agent/distributor selection process and regulatory requirements are sometimes not considered in the agent selection process. While some Chinese agents are knowledgeable and accountable to registration and certification requirements, most are unfamiliar with western standards of compliance, and are inexperienced with registration and certification requirements.

Regulatory affairs staff involved in compliance issues in China should become familiar with the current cultural and political issues in China. They should keep in mind that, as with some other Asian nations, it is not uncommon for regulatory authorities to play a role in domestic industry development, to have overlapping jurisdiction or contradictory requirements. Copies of regulations often are unavailable or available only in Chinese. Below are details on the central government authorities most relevant to the regulation of medical devices:

- In March 1998, the State Drug Administration (SDA) replaced the State Pharmaceutical Administration of China as the body responsible for exercising supervision and regulation over the processes of research, production, circulation and usage of drugs and medical devices. All medical devices imported to China from any nation must obtain a certificate issued by the government of the export country or a legitimate third party, and the certificate must attest to the safety and effectiveness of the product. Clinical testing data, type testing and quality systems inspections are not normally required of products that already have received approval in the country of manufacture. In other words, for goods manufactured in the US, FDA approval is accepted, and for goods manufactured in Europe, the CE Mark is accepted. However, SDA recently circulated a draft law, which will require type testing of all Class II and Class III devices, regardless of whether they are CE marked or FDA approved. The draft law also stipulates that implantable devices will have to undergo clinical testing in China, and manufacturing sites will be required to undergo Chinese quality systems inspections.
- If the medical device requires Chinese approval, SDA's regulations essentially are modeled on the EU system in that third-party organizations do the product testing based on international standards.
- China gradually has been adopting a safety quality licensing system of mandatory inspection and certification for imported goods that affect public safety, health and the environment. Certain medical devices fall under the State Administration for Import and Export Commodity Inspection (SACI) list including X-ray equipment, hemodialysis equipment, extracorporeal blood circuit and blood purification equipment, electrocardiographs, implantable cardiac pacemakers, and ultrasound diagnostic and therapy equipment. Many types of computer equipment that may be associated with medical devices also require SACI certification. Depending on the product, the safety licensing system requires any or all of the following: submission of product samples, design specifications, testing data and site inspections of each manufacturing plant. Underwriters Laboratories Inc. and TUV Rheinland China are two testing laboratories that have agreements with SACI, and can aid the certification process.

China is an example of a developing nation with a regulatory system in transition. The US Department of Commerce is encouraging China to improve transparency and eliminate redundancies, such as the safety quality licensing system discussed above.

Russia/Ukraine

Russia, Ukraine and the entire former Soviet Union represent a large potential future market. While the need is vast, resources for the purchase of medical products are scarce. However, as Russia and the rest of the region recover from the August 1998 financial crisis, revenue for purchasing medical products will increase. Also, plans to increase funds available through mandatory health insurance payroll taxes with both employer and employee contributions should result in more funds being available for medical products.

Russia and Ukraine are examples of difficult markets for US medical device firms to enter. Both nations have a non-transparent regulatory system that acts as a barrier for medical products. US exporters often are stymied in complying with rules and regulations to have their devices approved for sale. An FDA approval or CE Mark was not accepted since Russia and Ukraine do not automatically accept a device without doing their own testing and certification. US exporters found the non-transparency of the Russian and Ukraine regulatory systems very difficult. There is no guide, no set list of rules stating exactly what is needed. After months of complying with what they thought were the rules, US firms would discover upon submission that these rules had changed. In addition, the Russian or Ukrainian testing certification did not provide any positive benefits in terms of product safety.

Foreign firms must register their products with the

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Ministry of Health before selling medical devices in the Russian Federation. Registration requires clinical testing. If the Ministry of Health determines that the product may pose harm, a hygienic certification is required. Hygienic certification is a relatively new requirement, and the Ministry of Health is still determining appropriate costs and procedures. After registration and receipt of the Hygienic Certificate, the State Committee for Standardization, Metrology and Certification, GOSSTANDART, certifies that the device meets Russian standards and issues a Certificate of Conformance or GOST-R.

Bringing Russian standards into accordance, or harmonization, with international standards has not been fully accomplished, but the Russians have made some progress in this area. The US Department of Commerce and the American Chamber of Commerce in Moscow have worked very closely with Russian government officials to improve the transparency of regulatory systems. The Russian Ministry of Health and GOSSTANDART have been very active partners in this dialogue, and in July 1998 they published, for the first time, a step-by-step guide on the requirements for having medical devices properly registered and certified for sale in the Russian Federation. This guide — *Brochure on Registration and Certification Requirements for Medical Equipment and Devices Imported into the Russian Federation* — was funded by USAID. The Russian Federation has pledged its committment to ensuring the accuracy of the brochure with regular updates. This is a tangible example of improved transparency, and it can make a tremendous impact on the ability of US exporters to sell equipment to that market and for Russians to have access to some of the best medical technology available today.

The Ukrainian regulatory regime for medical devices is similar to Russia in that the rules for foreign products entering the market were similarly mysterious. Also like Russia, Ukraine is in the process of making major medical regulatory improvements, and the US Commerce Department has worked closely with the Ministry of Health and the American Chamber of Commerce in Ukraine to improve the system. Ukraine recently created a new National Agency on Quality Control and Safety of Food, Medicinal and Medical Use Products. The Director of this new agency has informed the Commerce Department that there are plans to overhaul Ukraine's entire medical regulatory process. New medical device regulatory procedures are being developed in line with the EU regulatory system, and these are being made available to US industry for comment prior to implementation through a process outlined in the joint documents issued by the Ukraine Ministry of Health and the US Commerce Department.

Brazil

The Brazilian market is large, with growing demand for US medical equipment. In 1998, the US shipped $300 million in medical devices to Brazil, the seventh largest medical market in the world. Brazil is developing a new regulatory system to improve the quality of healthcare offered to its citizens. Unfortunately, the regulations, as now understood, would limit access of Brazilian patients to modern medical technologies.

In late 1998, Brazil created a new FDA-like regulatory agency, the Brazilian National Sanitary Vigilance Agency (ANVS). Brazilian officials have worked closely with the US Commerce Department and FDA to ensure ANVS works effectively to protect the safety of Brazilian citizens, as well as efficiently to provide high quality, high technology medical equipment to its people in a timely manner. But US medical device firms have experienced difficulties penetrating the Brazilian market despite these efforts.

Brazil's public law implementing user fees has changed six times since it was first introduced earlier in 1999, creating uncertanties in the market and challenging regulatory affairs professionals. ANVA has reduced fees in response to industry pressure, but fees which cover product approvals and plant inspections remain quite high.

Lengthy review times also pose a problem for some US firms. Brazilian regulations state medical device approvals process should take no longer than 90 days. US medical device firms claim that in reality the process usually lasts six to 12 months. Some US medical device firms reported lost sales revenue in the millions due to the unduly long review process, not to mention the difficulties presented by constantly changing fees. Our feedback from US industry

is that the current Brazil medical device regulatory process could be improved with shorter review times and lower registration fees.

Despite these problems, the Brazilian market offers significant opportunities to US suppliers. Brazil is creating a modern regulatory health agency from the ground up. While that takes time, and while some disruptions and inefficiencies are to be expected, Brazilian officials have sought constructive dialogue with industry and the US government for long-term efficiencies. Brazil, along with other MERCOSUL member nations, recognizes the importance of harmonizing standards. By the end of 1999, MERCOSUL registration requirements are expected to supercede national requirements. Brazil participates in the Global Harmonization Task Force and this is a tremendous step forward. The ANVS Web site, http://svs.saude.gov.br, has useful information on legislation, technical departments and links to other sites — although all in Portuguese — that can help the US exporter.

Conclusion/Department of Commerce Activities

The summaries of the EU, Chinese, Russian/Ukrainian and Brazilian regulatory systems illustrate the different approaches nations take to regulate medical devices as well as how trade and regulation are interrelated. In general, open transparent regulatory systems will have better access to advanced medical technologies.

The Department of Commerce, through the International Trade Administration, is working actively in many countries in cooperation with US industry and FDA to improve their regulatory environment. The Commerce Department organized a series of seminars in September to promote the use of the Mutual Recognition Agreement by US medical device firms. In China, the Department has an ongoing dialogue with Chinese medical regulators through the US-China Joint Commission on Commerce and Trade (JCCT) Medical Subgroup. Commerce has worked closely with the China State Drug Administration to improve regulatory procedures, and China also was covered in the September seminar program. In Russia, the department actively works with the Russian Ministry of Health through a US-Russia Health Industries Business Development Subgroup, and in Ukraine the department works closely with the Ministry of Health through the US-Ukraine Committee on Trade and Investment. The US and Ukraine have signed a Medical Device Statement of Intent. In July 1999, the department aided a Brazilian congressional and judicial delegation in meeting with US government and industry officials involved in medical regulatory procedures. Follow-up activities with Brazil are anticipated.

The Commerce medical device Web site has short descriptions of the regulatory systems of a number of trading partners. The department encourages companies to use this resource when looking to confirm information or when planning market entrance strategies. Because regulations change frequently, the department invites regulatory affairs professionals to comment on conditions they experience, and to let us know of changes in regulatory requirements or procedures. This information also can help guide policy objectives.

The Department of Commerce also promotes US exports and has a vast array of programs to help US medical device firms export products. For example, trade missions are planned during 2000 and 2001 to China, Spain, Italy, Brazil, India, Central Europe, Taiwan, Australia, Singapore and Malaysia. The department also is promoting medical device exports through trade shows in Germany, Brazil, Argentina, Egypt, Thailand and Chile. For more information on any of these medical device activities, check the medical device homepage at http://www.ita.doc.gov/mdequip. The department has more than 90 domestic US Export Assistance Centers and more than 140 commercial offices in embassies and consulates around the world. A list of offices can be found at http://www.tradeinfo.doc.gov. These offices can provide a vast array of export assistance to medical device firms.

The global market for medical devices is expanding and emerging markets are growing faster than developed markets. As emerging nations improve their regulatory procedures, the global medical device market will be able to grow at an even faster rate. The Department of Commerce, and US medical device industry associations are working together to improve medical device market access and regulatory procedures. FDA has the lead role in regulatory activities and has demonstrated leadership in the Global Harmonization Task Force and the US-EU MRA.

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